



Lymphoedema surgery in Australia: a narrative review

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Background and Objective: Lymphoedema is a chronic condition that affects millions of people worldwide. It is often caused by the damage or removal of lymph nodes during cancer treatment. One of the most effective management options for lymphoedema is surgery, which can reduce swelling and potentially improve lymphatic drainage. Throughout history, Australia has been at the forefront of research and development in this field. In this review, we aim to examine the contributions of Australian research to lymphoedema surgery.

Methods: We conducted a search in the PubMed and Embase databases to identify Australian research relating to lymphoedema surgery from inception to the present day. Studies that met the inclusion criteria were reviewed and analysed, and the results were presented.

Key Content and Findings: After reviewing the literature, it was apparent that the field of lymphoedema surgery owes much to the contributions of Australian research. Early work from famous Australian surgeons such as Bernard O'Brien and Geoffrey Ian Taylor laid the bedrock for modern surgical techniques. Furthermore, more recently, Australia has seen a resurgence of clinical research contributing to the international evidence for lymphoedema surgery.

Conclusions: Australia has made significant contributions to the field of lymphoedema surgery, particularly in the development of modern microsurgical techniques such as lymphovenous anastomosis or vascularised lymph node transfer. These contributions have led to improved patient outcomes and quality of life. Going forward, Australia will hopefully continue to be a leader in research and innovation in this field.

Keywords: Lymphoedema surgery; Australia; lymphovenous anastomosis; microsurgery; vascularised lymph node transfer (VLNT)

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Introduction

Lymphoedema is a chronic, incurable, and significantly debilitating condition characterised by impaired lymphatic flow resulting in accumulation of lymphatic fluid in the

interstitial space (1,2). The condition can be classified as either primary, due to congenital dysfunction of the lymphatic system, or secondary, which, despite recent advances in management, most commonly occurs as

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a consequence of the management of malignancy in developed countries, particularly in the treatment of breast cancer (3-12). During such treatment, surgical removal of lymph nodes or adjuvant radiotherapy to the lymphatic system are the main aetiologies (13-17). Chronic lymphatic obstruction and stasis leads to dramatic oedema of affected areas which can cause discomfort for patients early in the course of the disease (18-20). Over time, chronic inflammation of the oedematous region results in progressive fibrosis and remodelling of the extracellular matrix along with adipose tissue deposition resulting in an irreversible increase in volume of the affected region (21-25). Furthermore, lymphoedema is unfortunately a relatively common condition, the incidence of which is often underestimated (26,27). Despite its common and debilitating nature, treatment for patients suffering from lymphoedema is often limited and ineffective.

Conservative approaches are the first line options for the treatment of lymphoedema and include various regimens of exercise, compression garments, bandaging and regular lymphatic massage (28-31). In addition, skin care and treatment of cutaneous infections such as cellulitis or erysipelas is an important aspect of long-term management (32). However, these approaches are based around management of the symptoms of lymphoedema and do not address the underlying lymphatic dysfunction. Hence, conservative treatment requires lifelong compliance from patients and poor adherence to management regimens significantly limits the effectiveness of treatment. Furthermore, in addition to conservative therapy, surgical management of lymphoedema offers an avenue to potentially correct the underlying physiology of the disease and offer further benefits for patients.

Surgical treatment of lymphoedema is often categorised into either reductive procedures, designed to remove the deposited subcutaneous fibroadipose tissue, or physiological procedures, which aim to restore lymphatic flow (33-37). These surgical options are often utilised alongside the conservative treatment modalities. Improvement in the modern understanding of lymphatic anatomy and advances in microsurgical technique has made such physiological procedures possible. Today, techniques such as vascularised lymph node transfer (VLNT) or lymphovenous anastomosis offer patients the hope of improving lymphatic function to target the root cause of lymphoedema (38-40). Furthermore, modern imaging techniques such as lymphoscintigraphy, ultra-high frequency ultrasound, indocyanine green angiography or near-infrared fluorescence imaging allows

for more accurate preoperative planning increases the chances of success (41).

Throughout history, Australian surgeons have contributed significantly to the development of lymphoedema surgery. In this review, we discuss the main surgical treatment modalities for lymphoedema, review and document the contribution of Australian research and innovation to the surgical management of lymphoedema and finally, describe the current state of lymphoedema surgery in Australia. We present this article in accordance with the Narrative Review reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/gs-23-181/rc>).

Methods

To identify Australian research contributions to the development of lymphoedema surgery a search was conducted in the PubMed and Embase databases from inception until the 6th of February 2023 (*Table 1*). The search was limited to studies published in English and to those conducted in Australia. Search criteria keywords in the contained within the title or abstract of the journal articles included the terms: (“Lymphoedema”) AND (“Lymphovascular anastomosis” OR “Lymphovenous anastomosis” OR “Lymphovenular anastomosis” OR “Lymphaticovascular anastomosis” OR “Lymphaticovenous anastomosis” OR “Lymphaticovenular anastomosis” OR “Lympho-lymphatic anastomosis” OR “Lymphovascular bypass” OR “Lymphovenous bypass” OR “Lymphovenular bypass” OR “Lymphaticovascular bypass” OR “Lymphaticovenous bypass” OR “Lymphaticovenular bypass” OR “Lympho-Lymphatic bypass” OR “Vascularised lymph node transfer” OR “Lymph node transfer” OR “Flap” OR “Liposuction” OR “Debulking” OR “Surgery” OR “Surgical”) AND (“Australia”). Furthermore, to add context to the discussion, a brief review of the main international literature pertaining to the main surgical management options of lymphoedema was conducted. This was achieved by a search in the same aforementioned databases. This search included combination of variations of the keywords: “Lymphoedema”, “Lymphovenous anastomosis”, “Lymph node transfer”, “Liposuction”, “Surgery” and “Surgical”. Additionally, key citations from previous reviews were checked for eligibility. Duplicate articles were removed. The title and abstract of each study were subsequently assessed for inclusion into the manuscript. Of the remaining studies, the full text was then screened for relevance to this review.

Table 1 The search strategy summary for inclusion of Australian research

Items	Specification
Date of search	6 th of February 2023
Databases and other sources searched	PubMed and Embase databases
Search terms used	("Lymphoedema") AND ("Lymphovascular anastomosis" OR "Lymphovenous anastomosis" OR "Lymphovenular anastomosis" OR "Lymphaticovascular anastomosis" OR "Lymphaticovenous anastomosis" OR "Lymphaticovenular anastomosis" OR "Lympho-lymphatic anastomosis" OR "Lymphovascular bypass" OR "Lymphovenous bypass" OR "Lymphovenular bypass" OR "Lymphaticovascular bypass" OR "Lymphaticovenous bypass" OR "Lymphaticovenular bypass" OR "Lympho-Lymphatic bypass" OR "Vascularised lymph node transfer" OR "Lymph node transfer" OR "Flap" OR "Liposuction" OR "Debulking" OR "Surgery" OR "Surgical") AND ("Australia")
Timeframe	Inception until 6 th of February 2023
Inclusion and exclusion criteria	<p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Studies published in English • Studies relating to the surgical management of lymphoedema or the development of surgical techniques for the treatment of lymphoedema • Studies conducted in Australia or had considerable input from Australian researchers from Australian institutions • All primary study designs were considered <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • Studies in languages other than English • Studies not relating to the surgical management of lymphoedema or the development of surgical techniques • Studies not conducted in Australia or had no input from Australian researchers • Conference abstracts, presentations or posters
Selection process	Studies were initially screened and selected independently by the first author and consensus regarding inclusion of all studies into the narrative review was obtained after discussion between all authors

Studies pertaining to Australia's contribution were included if they were conducted in an Australian institution or had heavy involvement from Australian researchers. A narrative synthesis approach was used to describe and compare the results of the studies included in the review. A summary of the main findings and key themes was provided.

Discussion

In patients with lymphoedema who have failed conservative approaches surgical management is warranted. Surgical options for lymphoedema can be broadly classified as one of two main categories: reductive techniques, which aim to reduce limb volume by removing subcutaneous tissue and physiological techniques which aim to improve/correct the underlying lymphatic function (34,37-39,42-44).

Furthermore, more recently, surgical management for lymphoedema may involve a combination of reductive and physiological techniques (45-48). The main physiological techniques used to treat lymphoedema include VLNT and lymphovenous anastomosis, while the main reductive techniques include liposuction and excisional procedures.

Australia has made significant contributions to the field of lymphoedema surgery since its conception, both in terms of research and clinical practice. Profound advances in microsurgical techniques, complex lymphatic anatomy and physiology, and pre-operative imaging stem from work conducted in Australia. Herein, we discuss the main surgical options available to treat lymphoedema, provide a concise overview of the international literature, and highlight the major contributions made by Australian surgeons towards their advancement.

Physiological techniques

Physiological techniques for lymphoedema aim to restore the underlying dysfunctional lymphatic anatomy. One such technique is lymphovenous anastomosis, which involves the connection of lymphatic vessels to small venules thereby bypassing the local obstructed lymphatic system and allowing lymph to flow through the venous system. Lymphovenous anastomosis was first described almost 60 years ago and since then the technique has developed considerably (49-51).

Several international studies have been conducted to assess the efficacy of lymphovenous anastomosis and many have shown promising results with reductions in limb volume and improvements in quality of life (52-55). Yet, the quality of evidence in many studies is somewhat limited by limitations such as small sample sizes and short follow-up periods (56-62). Furthermore, the use of lymphovenous anastomosis requires viable lymphatic anatomy with patent vessels, thus, it is thought to be less effective in the later stages of lymphoedema where irreversible fibrosis has occurred.

Another surgical option for the management of lymphoedema is VLNT. The technique involves the transplantation and anastomosis of vascularised tissue flaps containing lymph nodes to a recipient site near the affected region. It is thought that the transplanted healthy lymph node re-routes the lymph towards it, bypassing the obstruction (63,64). Additionally, it induces lymphangiogenesis at the recipient site, leading to development of new lymphatic channels over time (65-67). To date, numerous donor sites have been described as a source of healthy lymph nodes (68-71).

International evidence suggests that VLNT is also an effective surgical technique for the treatment of lymphoedema. Like lymphovenous anastomosis, studies have displayed significant reductions in volume and improvements in quality of life for patients (68,72-76). Furthermore, studies comparing lymphovenous anastomosis to VLNT have shown greater reductions in limb volume in the patients who received VLNT (77,78). An advantage of VLNT is that it does not require patent lymphatic vessels at the recipient site in order to offer benefit to patients. Additionally, it can sometimes be performed simultaneously at the time of microsurgical reconstruction, such as during breast reconstructive procedures using the deep inferior epigastric artery perforator flap (79,80). However, of note is the possibility of donor site secondary lymphoedema due to

the removal of healthy lymph nodes and lymphatic vessels from this area (81).

Near the advent of lymphoedema surgery, Australia was at the forefront of surgical research and development. Many of the currently available surgical techniques were pioneered by the famous Australian surgeon Bernard O'Brien and his colleagues at the Microsurgery Research Centre at St Vincent's Hospital in Melbourne. O'Brien was amongst the first to develop lymphovenous anastomosis as a surgical management option for patients with lymphoedema (82,83). His early experimental and clinical research made a profound contribution to the adoption of the technique worldwide (82-90). In 1976, O'Brien presented findings demonstrating a lasting improvement in lymphatic flow in dogs following lymphovenous anastomosis (82). Much of the understanding of the technique came from his early experimental work with canine models of lymphoedema (86,88,91). Finally, in 1990, O'Brien published the largest ever series of lymphovenous anastomoses among patients in Australia, describing in detail his results and surgical technique (90).

Furthermore, O'Brien and his colleagues also played a role in the early progress of lymph node transfer as a viable therapeutic option for lymphoedema (92-94). Again, using innovative canine models, O'Brien displayed the utility of lymph node transfer and its potential efficacy (89,92,94). Following on from O'Brien and his team, research about lymphoedema, its surgical management and its underlying physiology continued at this institution, now named the O'Brien institute, under O'Brien's successor Wayne Morrison (95-99).

Unfortunately, despite his significant contribution to the development of lymphatic microsurgery, O'Brien was reportedly disappointed with the results experienced by patients (100). Perhaps improvements in surgical outcomes required a refinement in the understanding of lymphatic anatomy. This anatomical research was led by renowned Australian surgeon, Professor Geoffrey Ian Taylor and his team at the University of Melbourne. The research conducted by Professor Taylor greatly advanced the knowledge of the anatomy of the lymphatic system, with detailed publications describing the lymphatic system in nearly all areas of the human body (101-111). Moreover, the discovery of the free flap by Professor Taylor was the catalyst of an enormous growth in microsurgical techniques (112,113). Furthermore, Taylor and his team played a role in the development of diagnostic and pre-operative imaging techniques of the lymphatic system for lymphoedema

(106,111,114-118). Inevitably, a greater understanding of human anatomy and more refined imaging techniques contributed to improvements in surgical outcomes for patients with lymphoedema.

More recently, Australia has been central to much clinical research evaluating lymphoedema microsurgery. Surgeons working at hospitals across Australia have begun to publish and present results of their experience at managing patients with lymphoedema. For instance, the Australian Lymphoedema Education and Research Treatment (ALERT) Programme at Macquarie University Hospital has demonstrated the effective use of a multi-disciplinary team in assessing and treating patients with lymphoedema (119). Moreover, the team at Macquarie University Hospital have recently published results of their treatment, contributing the growing bed of evidence for the microsurgical management of lymphoedema (119-122). Furthermore, various other institutions and surgeons across Australia have influenced clinical practice with novel descriptions of surgical techniques (123-126). Additionally, the O'Brien institute and St Vincent's Hospital in Melbourne remain a leader in Australian lymphoedema research and education under the direction of Ramin Shayan (98-100,127-129).

Ultimately, the Australian medical community has made, and continues to make, substantial contributions to the advancement and modernization of physiological surgical techniques for the treatment of lymphoedema. In the current day, lymphatic microsurgery is offered at numerous tertiary institutions across Australia, offering broad access to individuals suffering from the condition.

Reductive techniques

While physiological techniques are useful in restoring lymphatic function, the fibrotic and adipose tissue that deposits late in the course of lymphoedema cannot be removed by simply improving lymphatic flow in the affected area. In this setting, reductive techniques are required to remove dystrophic tissue and reduce swelling in the affected area. These are often used in conjunction with physiological techniques to achieve more impactful results. Reductive surgical options include either liposuction or excisional procedures.

Internationally, liposuction has repeatedly been shown to be an effective surgical treatment modality for patients suffering from lymphoedema, with studies displaying successful results in volume reduction, quality of life and long-term stability (130-133). Yet, one limitation is that it

has limited effect on correcting the underlying lymphatic dysfunction and therefore, patients are required to wear lifelong compression garments unless physiological procedures are also performed.

In advanced stage, severe fibrotic lymphoedema, excisional procedures may be necessary. Such procedures involve surgical removal of excess subcutaneous tissue and skin. The earliest excisional procedure used to manage lymphoedema was the Charles procedure described by Charles in 1912, which involved radical excision of all affected subcutaneous tissue and skin and coverage of wounds with split thickness skin grafts (134,135). Understandably, such a procedure resulted in significant morbidity and prolonged recovery time for patients. Over time this technique was modified, and numerous other techniques were established that utilised more conservative excision, such as the Homan technique, involving staged excision of subcutaneous tissue with preservation of the overlying skin (136-138). Some studies have reported encouraging outcomes for volume reduction using excisional procedures in the treatment of lymphoedema (139). However, most international evidence stems from retrospective or small prospective studies without a clear evidence base in long term prospective trials with large sample sizes (48,140-144).

Australia also played a role in the adoption of reductive techniques for the treatment of lymphoedema. Again, early work in this field can be attributed to O'Brien and colleagues at St Vincent's Hospital in Melbourne (85,97,145). In 1989, O'Brien published a case series of patients treated with liposuction, demonstrating an average reduction in limb volume of 23% (145). Subsequently, further promising results were reported by Morrison in 1990 where he reported on and compared both physiological and reductive techniques for treating lymphoedema (97). This seminal research carried out in Australia significantly influenced the utilization of liposuction for the treatment of lymphoedema.

Presently, researchers in Australia are once again making substantial progress in demonstrating the efficacy of these techniques. In conjunction with their work on microlymphatic surgery, research conducted by ALERT at Macquarie University Hospital has shown highly encouraging results regarding the use of liposuction for lymphoedema (119,146-149). They have demonstrated major reductions in limb swelling and improvements in quality of life, with low rates of complications following their interventions (119,146-149). For instance, a study conducted by Boyages *et al.* in 2015 reported an average

volume reduction of 89.6% in upper or lower limbs of their patients receiving liposuction (147). Again, some years later in 2020, in a multi-nation study including Australian patients and researchers, Klernäs *et al.* found significantly greater improvements in quality of life in the domains of physical, psychosocial and practical wellbeing in the patients receiving liposuction and compression therapy as compared to compression therapy alone (149). In modern day Australia, liposuction has evolved into one of the most frequently performed procedures for lymphoedema across the country. Its history of successful outcomes, combined with the lack of requirement for intricate microsurgical training, has made it an appealing technique for many plastic surgeons.

Despite the significant contributions to the field of liposuction, excisional procedures have received comparatively less attention in Australia. Apart from early reports by O'Brien and colleagues, the literature regarding the use of excisional methods from Australia is sparse (85,97). This likely stems from the fact that such procedures are associated with high risks of complications, including infection, wound dehiscence, poor cosmesis and decreased quality of life. Hence, these techniques are often reserved for advanced lymphoedema with significant fibrosis of the subcutaneous tissue where physiological methods and liposuction are likely to be ineffective. While excisional procedures may result in significant postoperative morbidity for patients, they remain warranted as a last line option in patients with refractory lymphoedema, unsuitable or unresponsive to other treatment modalities and are performed infrequently in Australia.

Conclusions

Lymphoedema surgery has made significant advancements in recent years and has become an effective option for those suffering from this debilitating condition. The Australian medical community has made significant contributions to the development of lymphoedema surgery and has been at the forefront of innovation and research in this field. With the growing recognition of the benefits of lymphoedema surgery, it is likely that we will see continued advances in the surgical techniques and treatments available to patients. As a result, more people around the world will be able to benefit from life-changing surgery, improving their quality of life and helping them lead more fulfilling lives. Australian surgeons should be proud of their role in the development of lymphoedema surgery and will hopefully continue to play a leading role in this field for many years to come.

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